REMARKS

Claims 1-22 are pending in this application. Claims 2-22 have been amended to obviate certain of the Examiner's objections to terms and antecedent basis, as more fully discussed below.

Claims 2-22 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserted that claims 2-10 and 12-19 were unclear in reciting "A device as in claim". Applicants believe the general phraseology employed in the claims is well accepted and proper, and clearly refers to the claim from which each depends. Thus, this aspect of the rejection may relate more to one of language of personal preference, rather than raise an issue of clarity. In any event, Applicants have adopted the Examiner's suggested phraseology and amended the claims accordingly, without intending any change in scope or meaning.

Claim 11 was rejected as unclear because the preamble recites preparing a vascular prosthesis, however the method steps refer to a vascular graft device. Further, the Examiner referred to the claim as incomplete because the method steps allegedly do not result in the producing the claimed product of a vascular prosthesis. The claim has been amended to substitute "graft" for "prosthesis," and to more clearly recite the product of the recited method steps.

Claim 15 has been amended to more clearly specify a gene encoding granulocyte colony stimulating factor "or" granulocyte macrophage colony stimulating factor.

Claim 19 was rejected as allegedly indefinite in the recitation of "glucose-regulated insulin or proinsulin polypeptide". Applicants have adopted Examiner's suggestion to delete "glucose-regulated," thereby obviating the basis of this rejection. In addition, "encoded" in line 2 was amended to "encodes."

Claim 20 was amended to delete reference to "prosthesis" and replaced with "graft," as previously discussed. In addition, the amendments clarify that the vascular endothelial cells and vascular smooth muscle cells are "obtained from a mammalian subject," to lend more clarity to the terms employed in claim 21.

Claim 21 was amended to substitute "culturing" for "cultivating," as kindly suggested by the Examiner. The amendments to claim 20 provide the antecedent basis for the other terms objected to by the Examiner.

Claim 22, alleged to be unclear in reciting "cultivating," has been amended to refer to "culturing," as in claim 21.

Based on the foregoing, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

Claims 1, 2, 4, 6, 11, 12 and 15 were rejected under 35 U.S.C. 102(a) as being anticipated by Osborne et al. The Office Action does not indicate which Osborne et al. reference is being relied on for this rejection. Applicants' representative has reviewed the file and believes the intended reference may be citation "BK" in the IDS submitted 12/27/94. Although the BK reference is referred to in the IDS and PTO-1449 as "Geary et al.," the first author is Osborne.

If this is the reference intended by the Examiner, it is not believed to be properly citable against the instant application as a §102(a) reference. The authors of Osborne et al., Osborne, Geary, Lau, Dale and Clowes, are identical to the inventors of the instant application: Osborne, Geary, Lau, Clowes and Dale, and the abstract is believed to describe aspects related to the instant invention. Thus, the publication does not describe an invention that was known or used by others in this country, as that language is used in 35 USC §102(a). Accordingly, if this is the reference the Examiner was relying on, the rejection should be withdrawn. In the event the Examiner intended a different reference, clarification is respectfully requested.

Applicants note the Office Action states on page 3 that "claims 11-22 stand rejected and claims 12-22 are newly rejected under 35 U.S.C. 112, first paragraph...." Yet, in the text on page 4 the Action states that "the rejection is also applied to claims 1-11." Clarification is respectfully requested.

Applicants note that the specification contains at least one working example, and additional working examples have been identified during the prosecution of the instant application. Applicants have previously made good faith arguments and amendments to the claims to address the Office's previous concerns as they relate to claims 12-22. Similar arguments would apply to claims 1-11, assuming they are encompassed by the present rejection. Thus, they believe the guidance provided by the specification is more than adequate to enable the presently claimed invention, and that the breadth of the enablement is commensurate with the scope of the claims. Applicants also note that other patents have issued in this field in the last few years which demonstrate that the art was more developed, and not as unpredictable, as urged by the Office. Accordingly, Applicants maintain their position on this issue as explained in previous responses, and reserve the right to pursue this in further proceedings as may be necessary.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: November 23, 2001

Steven W. Parmelee
Reg. No. 31,990

Customer No. 20350

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (206) 467-9600
Fax: (415) 576-0300
SWP/acg

SE 5010950 v1

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

1. (Twice Amended) A device for implanting autologous vascular smooth muscle cells transduced with a gene of interest into a mammalian subject, comprising:

a tubular elongate member having a wall, which wall has an interior surface, an exterior surface, and pores therein; and

autologous smooth muscle cell transduced with the gene of interest immobilized within the pores and upon the interior surface of the wall to form a tubular smooth muscle cell complex whereby the smooth muscle cells remain stably immobilized on the graft surface and express a product of said gene.

2. (Once Amended) [A] The device [in] of claim 1, wherein the tubular elongate member is comprised of a porous synthetic material.

3. (Once Amended) [A] The device [as in] of claim 2, wherein the porous synthetic material is polytetrafluoroethylene (PTFE), dacron or nylon.

4. (Once Amended) [A] The device [as in] of claim 3, wherein the tubular elongate member is a vascular graft.

5. (Once Amended) [A] The device [as in] of claim 1, wherein the autologous vascular smooth muscle cells are transduced with a gene encoding erythropoietin.

6. (Twice Amended) [A] The device [as in] of claim 1, wherein the autologous vascular smooth muscle cells are transduced with a gene encoding granulocyte colony stimulating factor or granulocyte macrophage colony stimulating factor.

7. (Twice Amended) [A] The device [as in] of claim 1, wherein the autologous vascular smooth muscle cells are transduced with a gene encoding Factor IX.

8. (Twice Amended) [A] The device [as in] of claim 1, wherein the transduced autologous vascular smooth muscle cells express an anticoagulant.

9. (Once Amended) [A] The device [as in] of claim 1, wherein the transduced autologous vascular smooth muscle cells are immobilized to the tubular elongate member with a polymer.

10. (Twice Amended) [A] The device [as in] of claim 1, wherein the device, prior to implantation in a subject, further comprises autologous vascular endothelial cells adherent to an interior surface of the tubular smooth muscle cell complex.

11. (Thrice Amended) A method for preparing a vascular [prosthesis] graft seeded ex vivo with vascular smooth muscle cells transduced to express a gene of interest, comprising the steps of:

transducing mammalian vascular smooth muscle cells with the gene of interest operably linked to a promoter for expression;

and immobilizing the transduced vascular smooth muscle cells on a vascular graft surface, whereby the smooth muscle cells remain stably immobilized on the graft surface and express a product of said gene, thereby producing said vascular graft having vascular smooth muscle cells transduced to express a gene of interest.

12. (Once Amended) [A] The method [as in] of claim 11, wherein the gene encodes erythropoietin, granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, or Factor IX.

13. (Thrice Amended) [A] The method [as in] of claim 11, wherein the gene encodes erythropoietin.

14. (Thrice Amended) [A] The method [as in] claim 11, wherein the gene encodes Factor IX.

15. (Thrice Amended) The method of claim 11, wherein the gene encodes granulocyte colony stimulating factor[,] or granulocyte macrophage colony stimulating factor.

16. (Thrice Amended) [A] The method [as in] of claim 11, wherein the transduced cells constitutively express an anticoagulant protein.

17. (Once Amended) [A] The method [as in] of claim 16, wherein the anticoagulant is a plasminogen activator or antithrombin-III.

18. (Once Amended) [A] The method [as in] of claim 17, wherein the plasminogen activator is alteplase or urokinase.

19. (Four Times Amended) [A] The method [as in] of claim 11, wherein the gene of interest [encoded glucose-regulated] encodes insulin or proinsulin polypeptide, and wherein the transduced cells express [glucose-regulated] insulin or proinsulin polypeptide.

20. (Thrice Amended) A method for preparing a vascular [prosthesis] graft device seeded ex vivo with vascular smooth muscle cells transduced to express a protein product, comprising the steps of:

culturing vascular endothelial cells and vascular smooth muscle cells obtained from a mammalian subject;

transducing the smooth muscle cells with a gene which encodes the protein product, operably linked to a promotor;

immobilizing on a tubular elongate porous vascular graft device the transduced smooth muscle cells within the pores and interior surface of the graft device; and

coating the interior of the graft device having immobilized thereon the transduced smooth muscle cells with the endothelial cells.

21. (Thrice Amended) The method of claim 20, further comprising the step of [cultivating] culturing the vascular smooth muscle cells obtained from a mammalian subject in a medium containing autologous serum prior to immobilizing the cells on the vascular graft device.

22. (Twice Amended) The method of claim 21, further comprising the step of [cultivating] culturing the vascular endothelial cells obtained from a mammalian subject in a medium containing autologous serum prior to coating the vascular graft device.